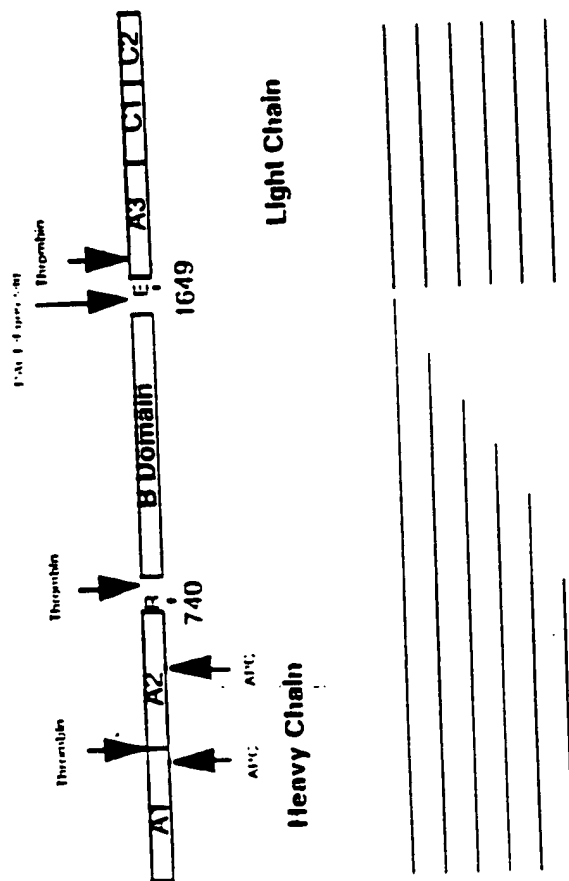


FIG. 1

$\Gamma_{\text{eff}}^{(0)}, \Gamma_{\text{eff}}^{(1)}$, from eqs. (9), (10) are



Heterogeneity of hFVIII is due to proteolysis within the B-domain

FIG. 2

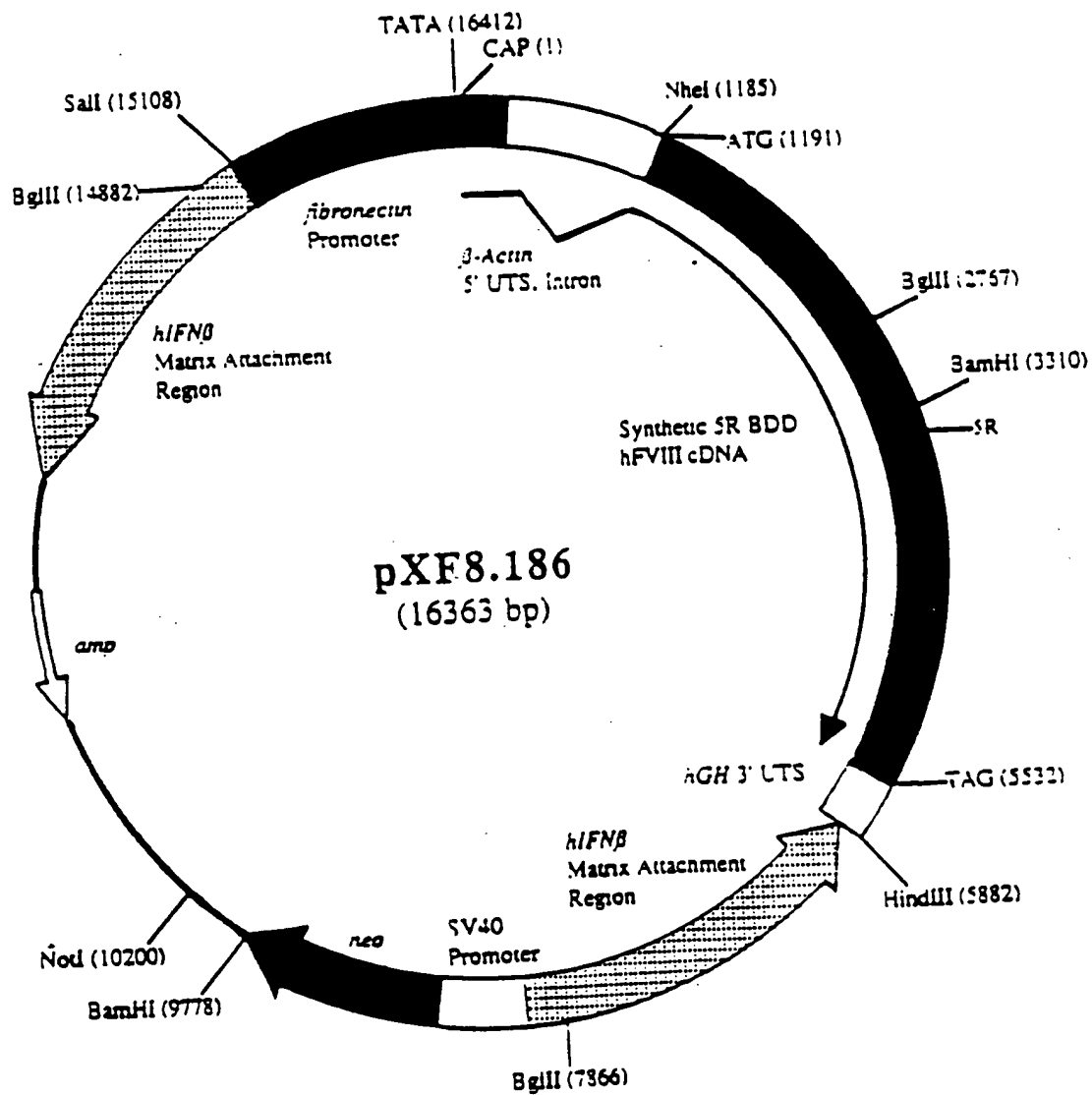


FIG. 3

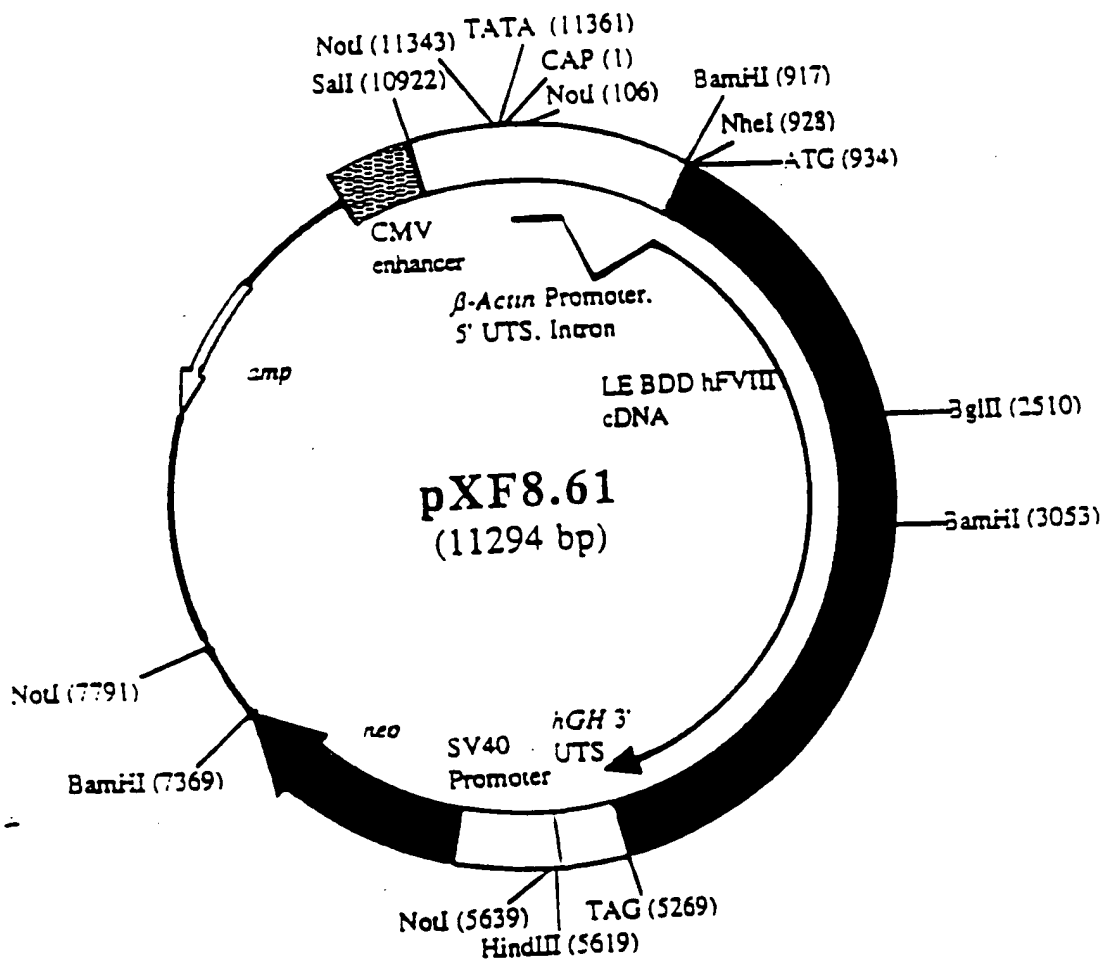


FIG. 4

Fragment B

FIG. 5 (2 of 14)

Fragment C

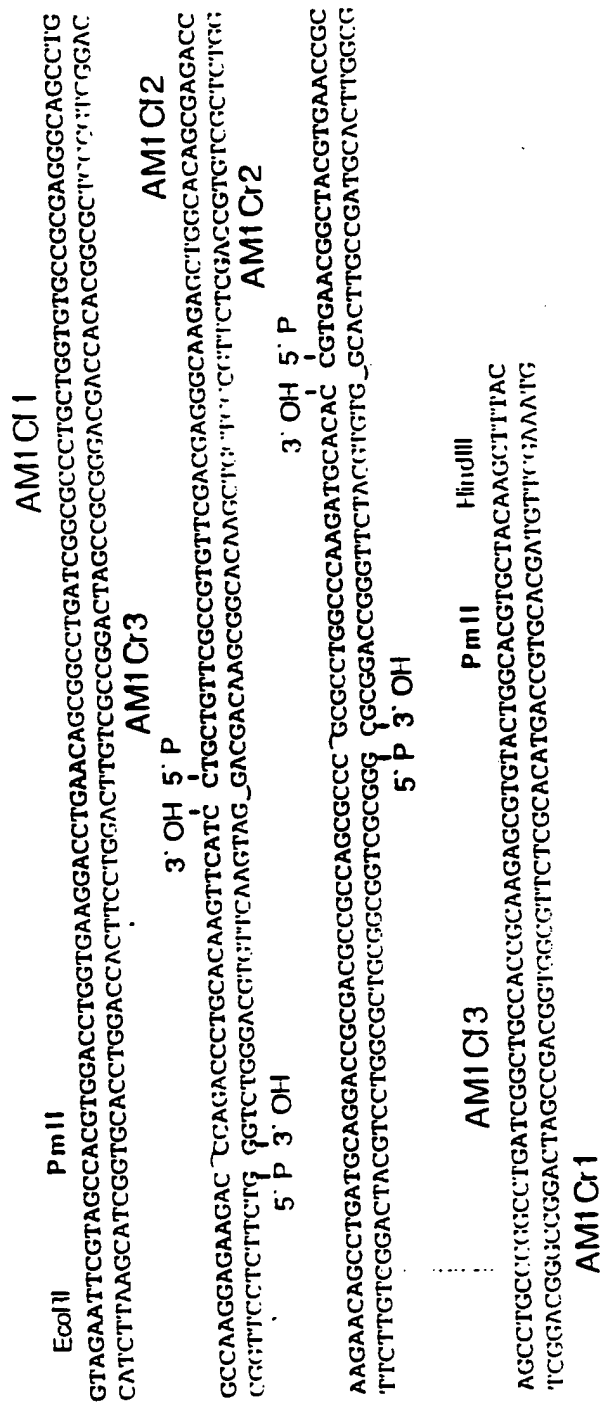


FIG. 5 (3 of 14)

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FIG. 5 (4 of 14)

1. The first group of people who are interested in the study of the history of the world are the historians. They are the people who study the past and try to understand what happened and why it happened. They use a variety of sources, including books, documents, and artifacts, to reconstruct the past.

FIG. 5 (5 of 14)

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FIG. 5 (6 of 14)

[illegible]

FIG. 5 (7 of 14)

Fragment H

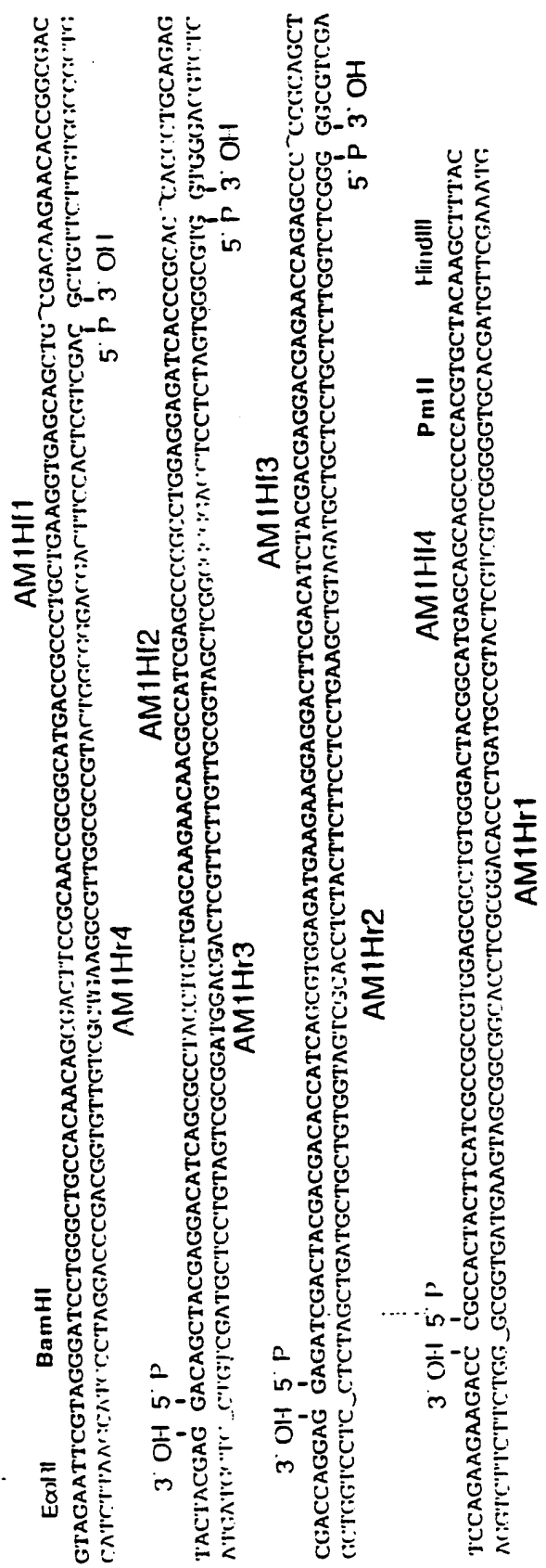


FIG. 5 (8 of 14)

Fragment I

EcoII PmlI
 (T)AGAA(TTCGTAGCACGTGCTGGCAACCGCGCCACAGAGTCCAGAGGTTCAAGAAAGTGGTGTTCAGGAGTTCAACGACGGCAGCTTCACCCAG
 CATCTTAAGCATCTGTGCACGCGCTTGGCGGGGTCTN:G:GTGTCGACGGGTCAAGTTCCTTCCACCACTAAGGTCTCTAAGTGGCTGCCGTTC PAAAGTGGGCTC
 5' P 3' OH
 AM1111
 BstEII
 AM1112
 Apal
 AM1113
 AM11r3
 3' OH 5' P
 CCCCCTGTACCGC GCGAGCTGAACGAGCACCTGGGCTCTCTCGGCCCTTACATCCGCGCGAGGTGGAGAGGACAAACATCATGGTGACCGTGCAGGATTTCGTC
 CTTGACATGGCG_CCGGCTCTACCTCTCTCGTGTGACCCCG:NT:ACCCGGGGATGTAGCGCGGTCCACCTCTCTCTTAGTACCACCTTCCAGCTTCTCTTAGTACCAGCTGG
 5' P 3' OH
 AM1114
 KpnI
 AM11r4
 3' OH 5' P
 TTCAAGGAGAACTACCGCTTCCACG CCATCAACGGCTACATCATGGACACCTTGGTGTATGGCCAGGACCGCATCCGCTGGTACCCCTACAA
 AATTTCTCTTGTGATGGCGAAGGTGC_GGTAGTTGCCGATCTAGTACCTGTGGGACGGCCGGACCACTACCGGGTCTCTGGTCGGTAGGCGACCAATGGGATGT
 AM11r1
 GCTTTAC
 CCAAAATG

FIG. 5 (9 of 14)

Fragment J

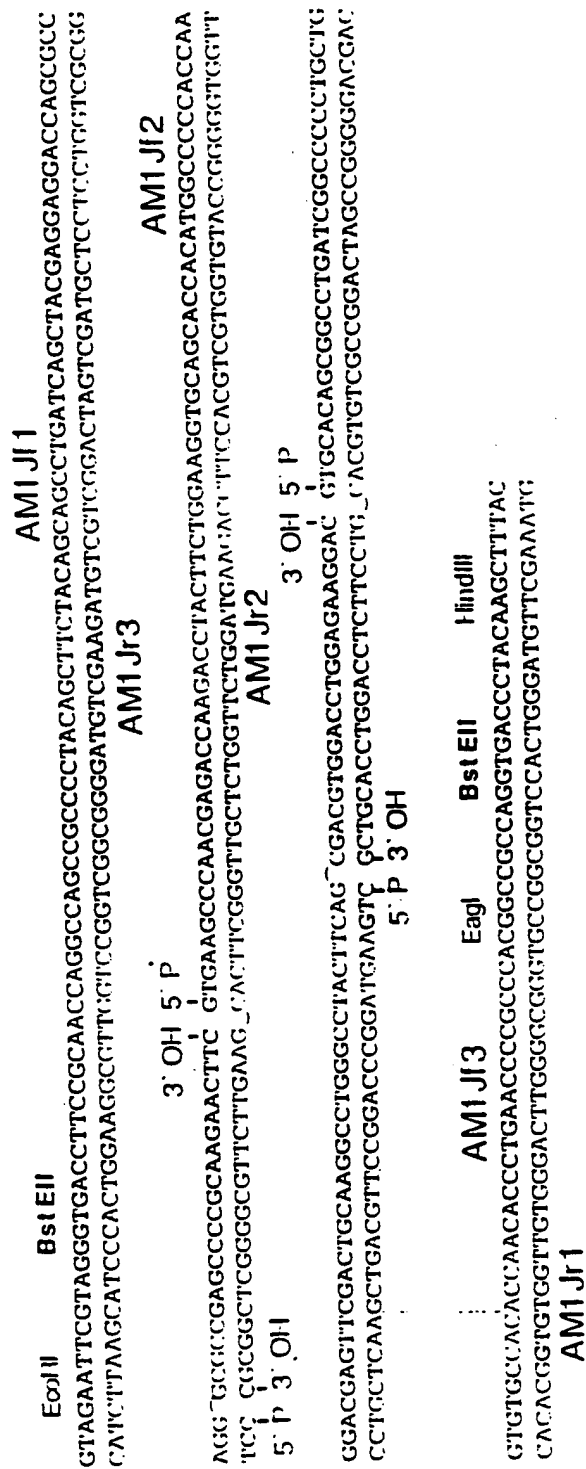


FIG. 5 (10 of 14)

Fragment K

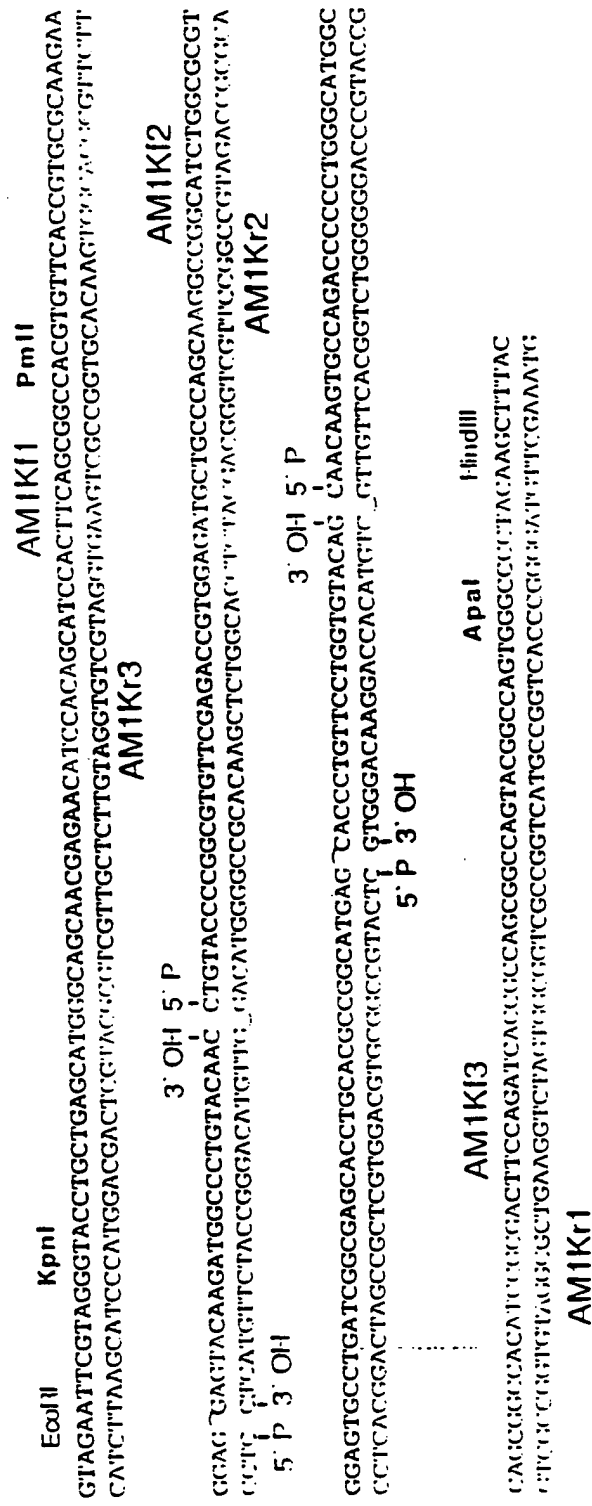


FIG. 5 (11 of 14)

Fragment L

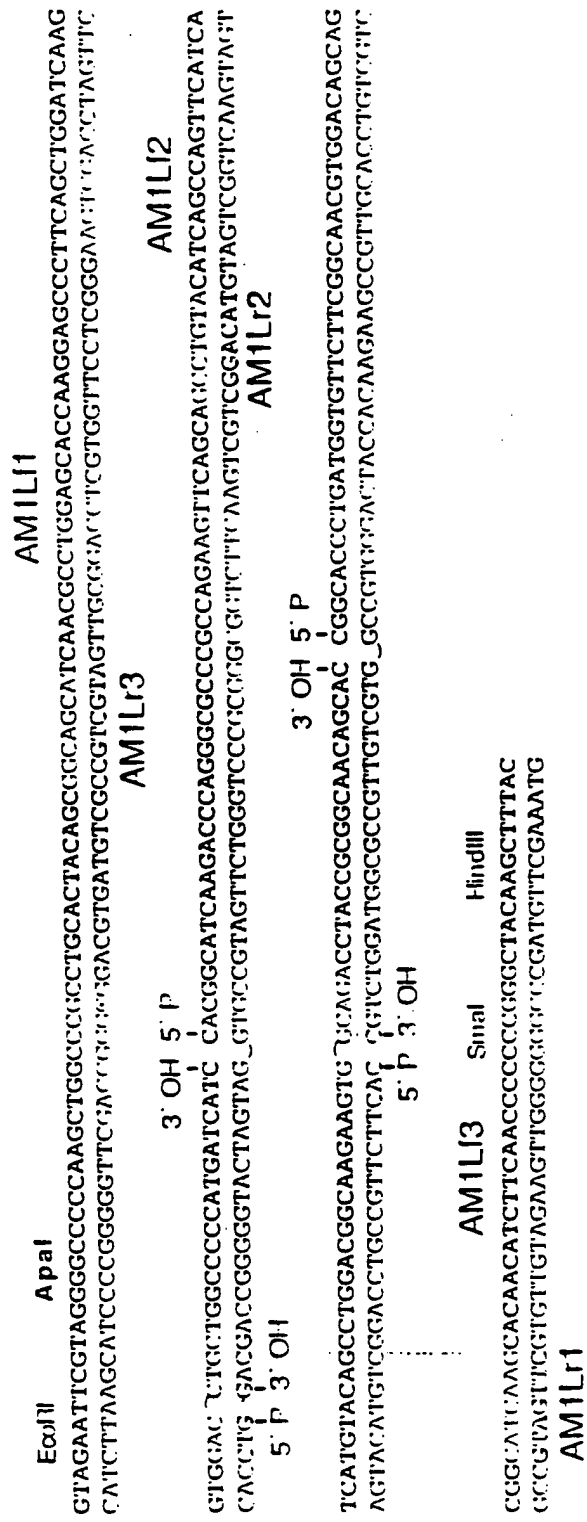


FIG. 5 (12 of 14)

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FIG. 5 (13 of 14)

Fragment N

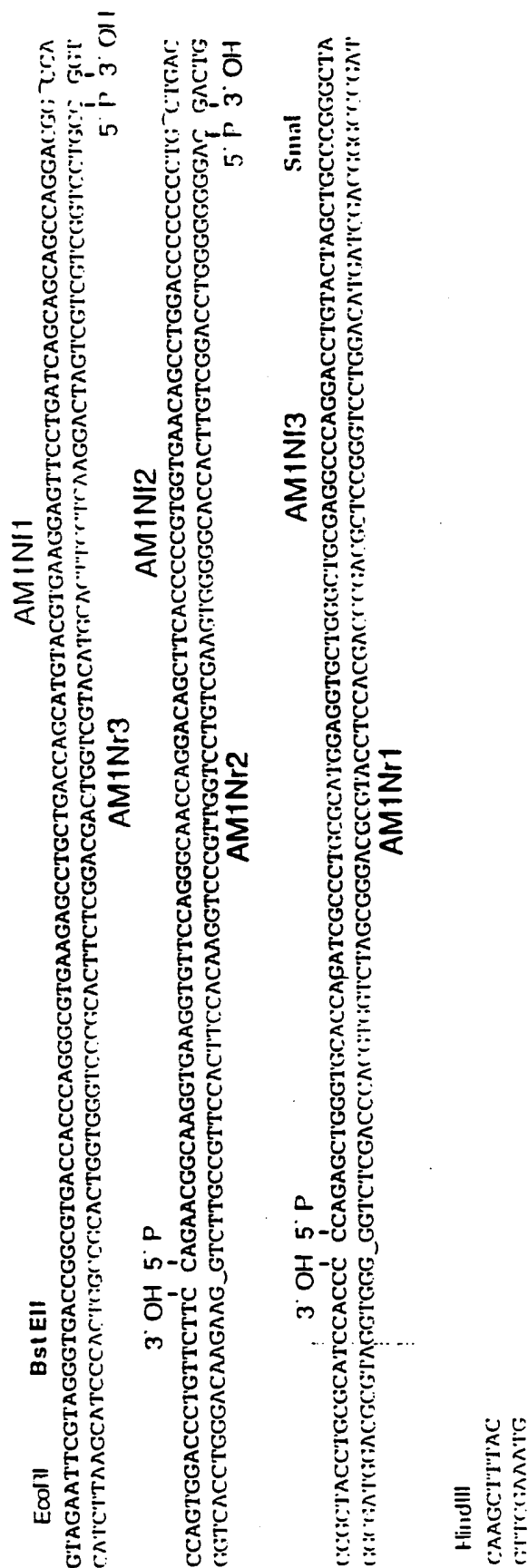


FIG. 5 (14 of 14)

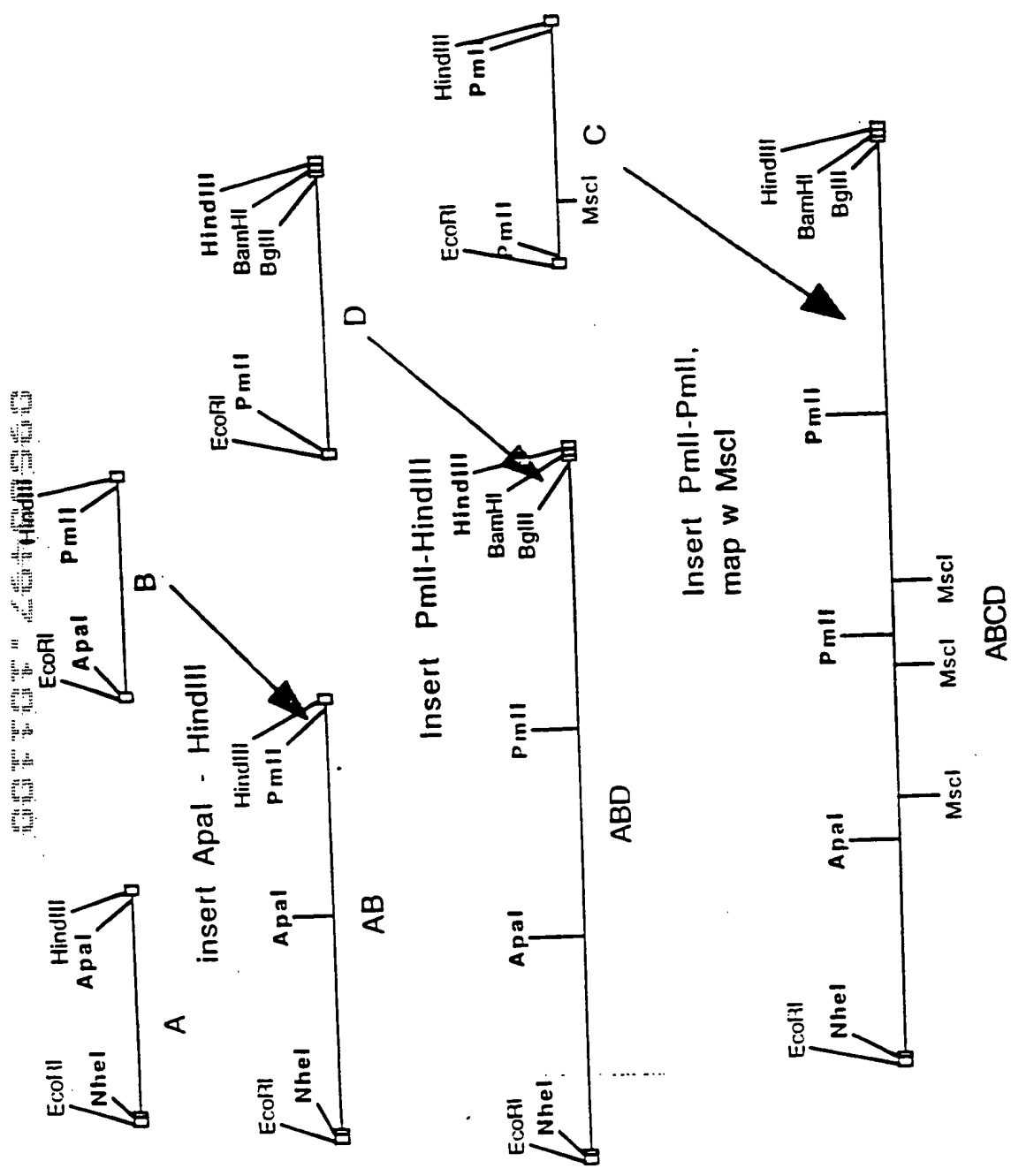


FIG. 6 (1 of 5)

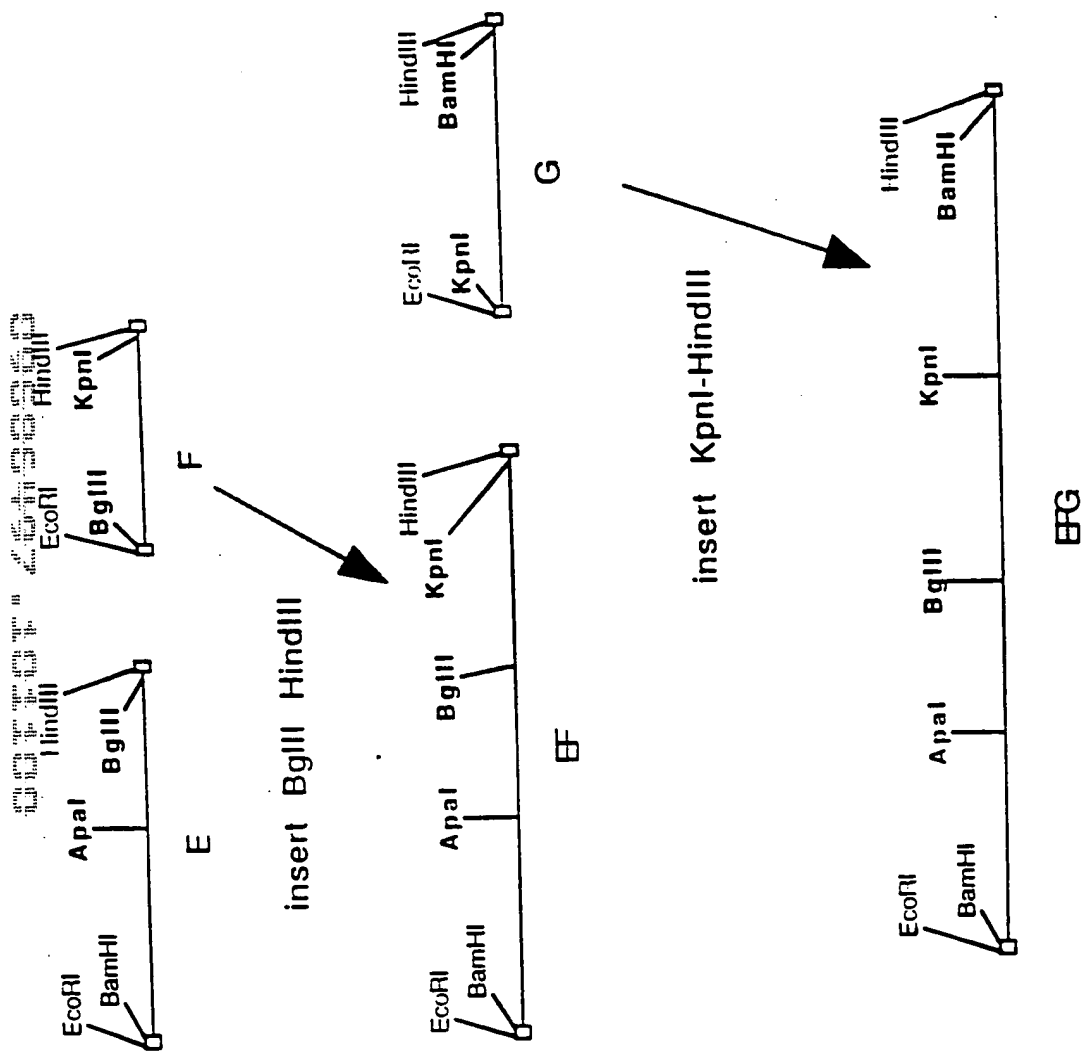


FIG. 6 (2 of 5)

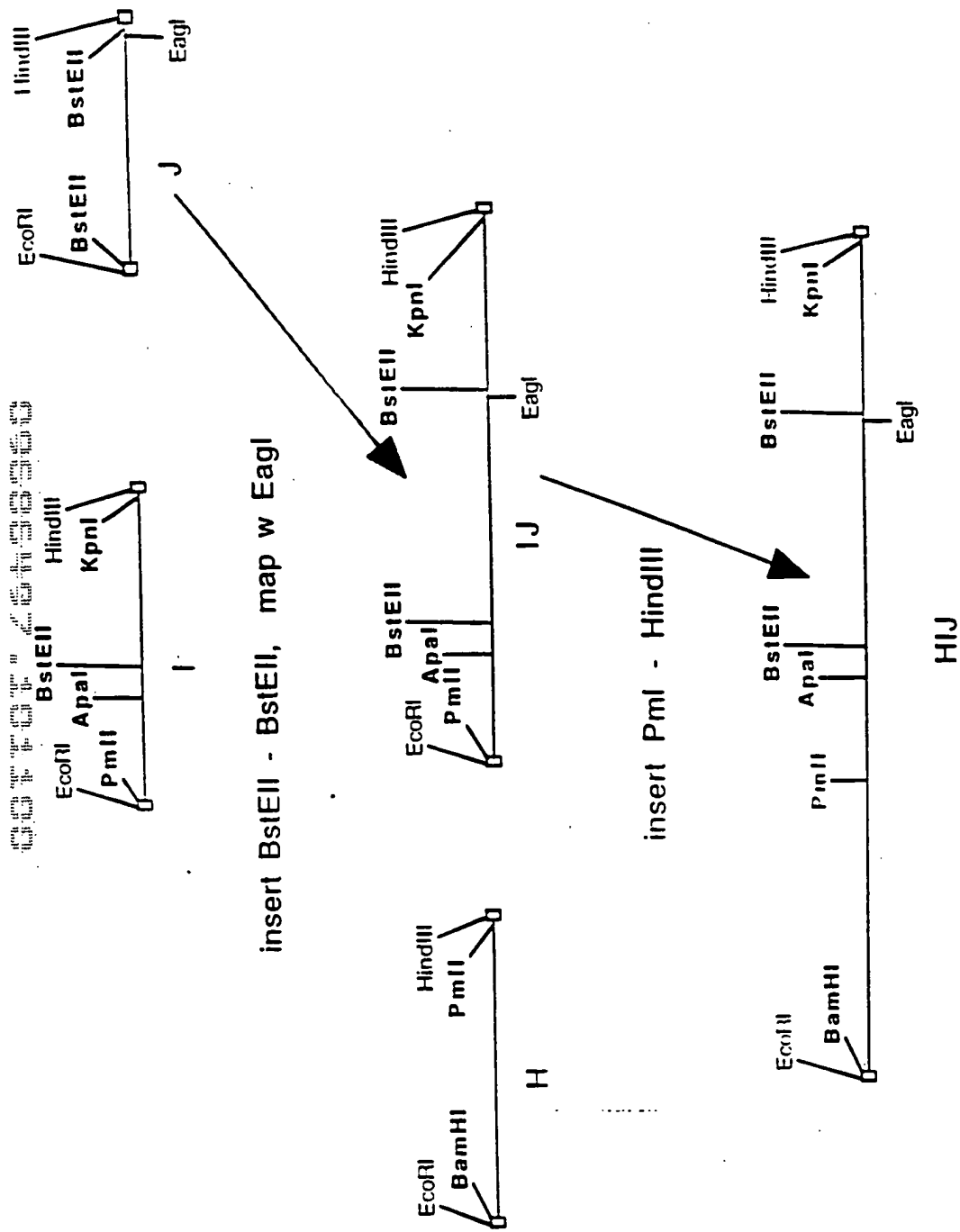


FIG. 6 (3 of 5)

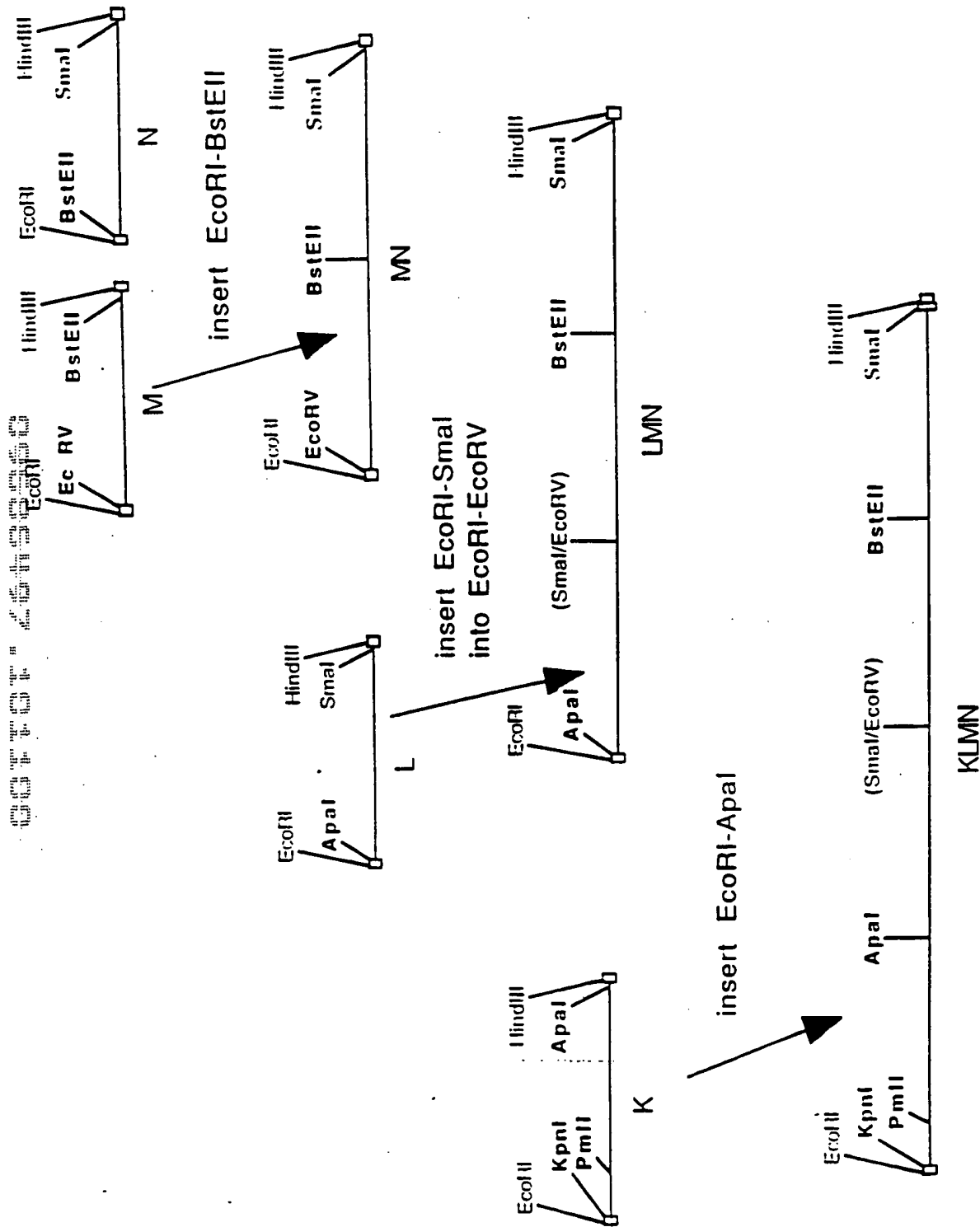


FIG. 6 (4 of 5)

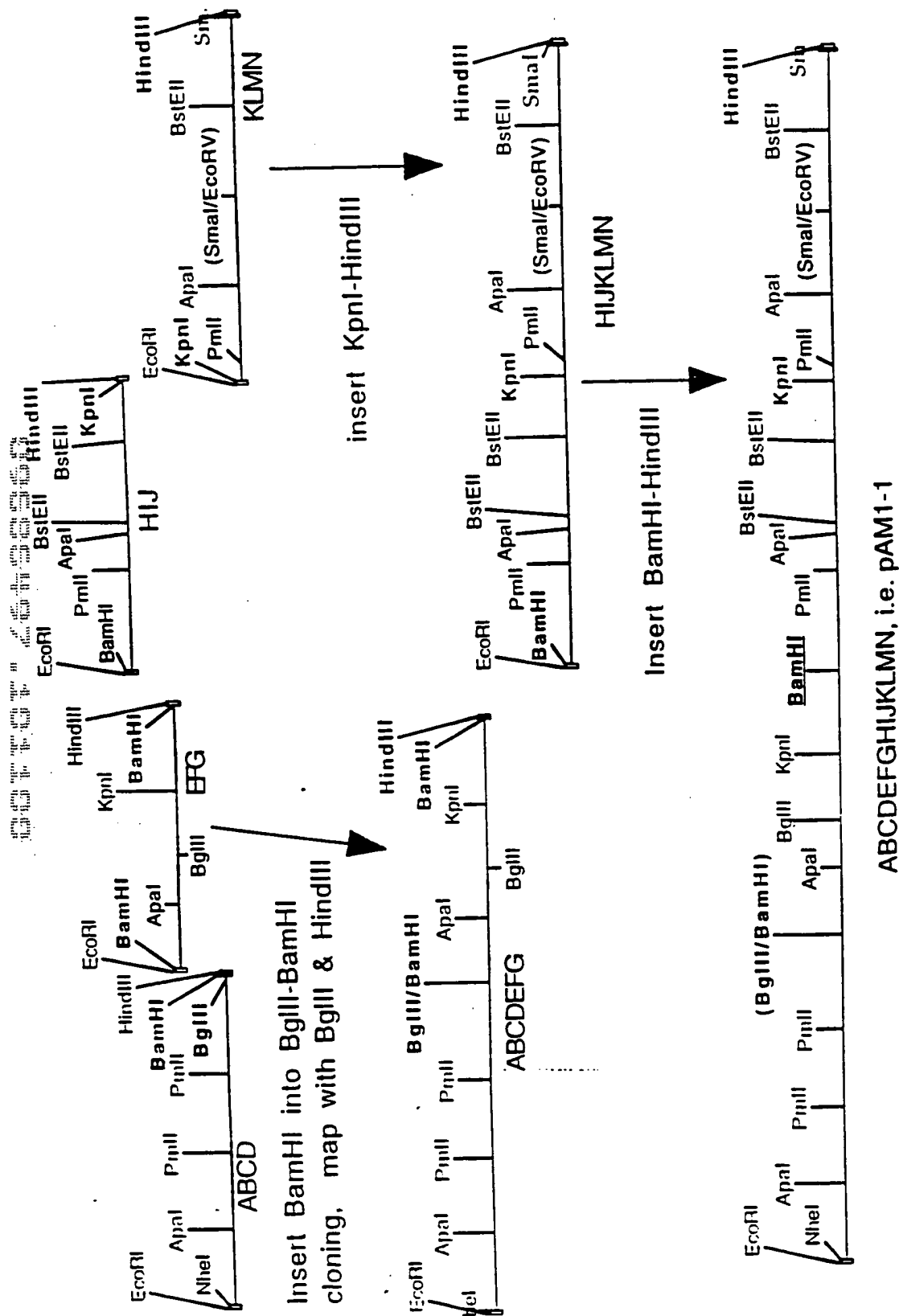


FIG. 6 (5 of 5)

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1 TAGAATTCGTTAGGCTAGCATCCAGATCGAGCTCAGCACCTGCTTCTCTCTGCGCTGCTGCGGCTTCTGCTTC
131 MetGlnIleGluLeuSerThrCysPhePheLeuCysLeuLeuArgPheCysPhe

73 AGCGCCACCCGCGCTACTACCTGGGCGCCCTGGAGCTGAGCTGGGACTACATGCAGAGCGACCTGGGCGAG
19 SerAlaThrArgArgTyrTyrLeuGlyAlaValGluLeuSerTrpAspTyrMetGlnSerAspLeuGlyGlu
145 CTGCCCGTGGACGCCCGCTTCCCCCCCCCGCTGCCCAAGAGCTTCCCTTCAACACCAGCGTGGTGTACAAG
43 LeuProValAspAlaArgPheProProArgValProLysSerPheProPheAsnThrSerValValTyrLys
217 AAGACCCTGTTCGTGGAGTTCACCGACCACCTGTTCAACATCGCCCAAGCCCCGCCCCCCTGGATGGGCCTG
67 LysThrLeuPheValGluPheThrAspHisLeuPheAsnIleAlaLysProArgProProTrpMetGlyLeu

Apal MscI

289 CTGGGCCCCACCATCCAGGCGGAGGTGTACGACACCGTGGTGTATCACCCTGAAGAATGCGCCAGCCACCCC
91 LeuGlyProThrIleGlnAlaGluValTyrAspThrValValIleThrLeuLysAsnMetAlaSerHisPro
361 GTGAGCCTGCACGCCGTGGGCGTGAGCTACTGGAAGGCCAGCGAGGGCGCCGAGTACGACGACCAGACCAGC
115 ValSerLeuHisAlaValGlyValSerTyrTrpLysAlaSerGluGlyAlaGluTyrAspAspGlnThrSer
433 CAGCGCGAGAAGGAGGACGACAAGGTGTTCCCCGGCGGCAGCCACACCTACGTGTGGCAGGTGCTGAAGGAG
139 GlnArgGluLysGluAspAspLysValPheProGlyGlySerHisThrTyrValTrpGlnValLeuLysGlu

MscI PmlI

505 AACGGCCCCATGGCCAGCGACCCCTGTGCCTGACCTACAGCTACCTGAGCCACGTGGACCTGGTGAAGGAC
163 AsnGlyProMetAlaSerAspProLeuCysLeuThrTyrSerTyrLeuSerHisValAspLeuValLysAsp

MscI

577 CTGAACAGCGGCCTGATCGGCGCCCTGCTGGTGTGCCGCGAGGGCAGCCCTGGCCAAGGAGAAGACCCAGACC
187 LeuAsnSerGlyLeuIleGlyAlaLeuLeuValCysArgGluGlySerLeuAlaLysGluLysThrGlnThr
649 CTGCACAAGTTCATCCTGCTGTTCCGCGTGTTCGACGAGGGCAAGAGCTGGCACAGCGAGACCAAGAACAGC
211 LeuHisLysPheIleLeuLeuPheAlaValPheAspGluGlyLysSerTrpHisSerGluThrLysAsnSer
721 CTGATGCAGGACCGCGACGCGCCGACGCGCCCGCGCCTGGCCCAAGATGCACACCGTGAACGGCTACGTGAAC
235 LeuMetGlnAspArgAspAlaAlaSerAlaArgAlaTrpProLysMetHisThrValAsnGlyTyrValAsn

PmlI

793 CGCAGCCTGCCCCGGCCTGATCGGCTGCCACCGCAAGAGCGTGTACTGGCACGTGATCGGCATGGGCACCACC
259 ArgSerLeuProGlyLeuIleGlyCysHisArgLysSerValTyrTrpHisValIleGlyMetGlyThrThr
865 CCCGAGGTGCACAGCATCTTCCTGGAGGGCCACACCTTCCTGGTGGCGCAACCACCGCCAGGCCAGCCTGGAG
283 ProGluValHisSerIlePheLeuGluGlyHisThrPheLeuValArgAsnHisArgGlnAlaSerLeuGlu
937 ATCAGCCCCATCACCTTCCTGACCGCCGACCCCTGCTGATGGACCTGGGCGAGTTCCTGCTGTTCTGCCAC
307 IleSerProIleThrPheLeuThrAlaGlnThrLeuLeuMetAspLeuGlyGlnPheLeuLeuPheCysHis
1009 ATCAGCAGCCACCAGCAGCAGCGCATGGAGGCCCTACGTGAAGGTGGACAGCTGCCCCGAGGAGCCCCAGCTG
331 IleSerSerHisGlnHisAspGlyMetGluAlaTyrValLysValAspSerCysProGluGluProGlnLeu
1081 CGCATGAAGAACAACGAGGAGGCCGAGGACTACGACGACGACCTGACCGACAGCGAGATGGACGTGGTGGCG
355 ArgMetLysAsnAsnGluGluAlaGluAspTyrAspAspAspLeuThrAspSerGluMetAspValValArg

(BglII/BamHI)

1153 TTCGACGACGACAACAGCCCCAGCTTCATCCAGATCCGACGCGTGGCCAAGAAGCACCCCCAAGACCTGGGTG
379 PheAspAspAspAsnSerProSerPheIleGlnIleArgSerValAlaLysLysHisProLysThrTrpVal
1225 CACTACATCGCCGCGGAGGAGGAGGACTGGGACTACGCCCCCCTGGTGTGGCCCCCGACGACCGCAGCTAC
403 HisTyrIleAlaAlaGluGluGluAspTrpAspTyrAlaProLeuValLeuAlaProAspAspArgSerTyr

EagI

1297 AAGAGCCAGTACCTGAACAACGGCCCCCAGCGCATCGGCCGCAAGTACAAGAAGGTGCGCTTCATGGCCTAC
427 LysSerGlnTyrLeuAsnAsnGlyProGlnArgIleGlyArgLysTyrLysLysValArgPheMetAlaTyr

Apal

1369 ACCGACGAGACCTTCAAGACCTGGGAGGCCATCCAGCAGCAGAGCGCGCATCCTGGGCCCCCTGCTGTACGGC
451 ThrAspGluThrPheLysThrArgGluAlaIleGlnHisGluSerGlyIleLeuGlyProLeuLeuTyrGly

FIG. 7 (1 of 3)

1441 CAGGTGGGCGACAGCCCTGCTGATCATCTTCAAGAACCAGGCCAGCCSCCCTACAACATCTACCCCCACGGC
 475> GluValGlyAspThrLeuLeuIleIlePheLysAsnGlnAlaSerArgProTyrAsnIleTyrProHisGly
 1513 ATCACCAGCGTGCSCCCCCCTGTACAGCCCGCCCTGCCCAAGGGCGTGAAGCACCTGAAGGACTTCCCCATC
 499> IleThrAspValArgProLeuTyrSerArgArgLeuProLysGlyValLysHisLeuLysAspPheProIle

BglII

1585 CTGCCCCGCGAGATCTTCAAGTACAAGTGGACCGTGACCGTGGAGGACGGCCCCACCAAGAGCGACCCCGCG
 523> LeuProGlyGluIlePheLysTyrLysTrpThrValThrValGluAspGlyProThrLysSerAspProArg
 1657 TGCCTGACCCGCTACTACAGCAGCTTCGTGAACATGGAGCGCGACCTGGCCAGCGGCCTGATCGGCCCCCTG
 547> CysLeuThrArgTyrTyrSerSerPheValAsnMetGluArgAspLeuAlaSerGlyLeuIleGlyProLeu
 1729 CTGATCTGCTACAAGGAGAGCGTGGACCAGCGCGCAACCAGATCATGAGCGACAAGCGCAACGTGATCCTG
 571> LeuIleCysTyrLysGluSerValAspGlnArgGlyAsnGlnIleMetSerAspLysArgAsnValIleLeu

KpnI

1801 TTCAGCGTGTTCGACGAGAACCCGACGCTGGTACCTGACCGAGAACATCCAGCGCTTCTGCCCAACCCCGCC
 595> PheSerValPheAspGluAsnArgSerTrpTyrLeuThrGluAsnIleGlnArgPheLeuProAsnProAla
 1873 GCGGTGCAGCTGGAGGACCCCGAGTTCCAGGCCAGCAACATCATGACACAGCATCAACGGCTACGTGTTTCGAC
 619> GlyValGlnLeuGluAspProGluPheGlnAlaSerAsnIleMetHisSerIleAsnGlyTyrValPheAsp
 1945 AGCCTGCAGCTGAGCGTGTGCTTCCAGAGGTGGCCTACTGGTACATCCTGAGCATCGGCGCCAGACCGAC
 643> SerLeuGlnLeuSerValCysLeuHisGluValAlaTyrTrpTyrIleLeuSerIleGlyAlaGlnThrAsp
 2017 TTCCTGAGCGTGTTCCTCAGCGGCTACACCTTCAAGCACAAGATGGTGTACGAGGACACCCTGACCCTGTTC
 667> PheLeuSerValPhePheSerGlyTyrThrPheLysHisLysMetValTyrGluAspThrLeuThrLeuPhe

BamHI

2089 CCCTTCAGCGCGGAGACCGTGTTCATGAGCATGGAGAACCCCGGCTGTGGATCCTGGGCTGCCACAACAGC
 691> ProPheSerGlyGluThrValPheMetSerMetGluAsnProGlyLeuTrpIleLeuGlyCysHisAsnSer
 2161 GACTTCCGCAACCCCGGCATGACCGCCCTGCTGAAGGTGAGCAGCTGCGACAAGAACACCGGCGACTACTAC
 715> AspPheArgAsnArgGlyMetThrAlaLeuLeuLysValSerSerCysAspLysAsnThrGlyAspTyrTyr
 2233 GAGGACAGCTACGAGGACATCAGCGCCTACCTGCTGAGCAAGAACAACGCCATCGAGCCCCCGCTGGAGGAG
 739> GluAspSerTyrGluAspIleSerAlaTyrLeuLeuSerLysAsnAsnAlaIleGluProArgLeuGluGlu

BstXI

2305 ATCACC CGCACCACCTGCAGAGCGACCGAGGAGATCGACTACGACGACCCATCAGCGTGGAGATGAAG
 763> IleThrArgThrThrLeuGlnSerAspGlnGluGluIleAspTyrAspAspThrIleSerValGluMetLys
 2377 AAGGAGGACTTCGACATCTACGACGAGGACGAGAACCAGAGCCCCCGCAGCTTCCAGAAGAAGACCCGCCAC
 787> LysGluAspPheAspIleTyrAspGluAspGluAsnGlnSerProArgSerPheGlnLysLysThrArgHis

PmlI

2449 TACTTCATCGCCCGCGTGGAGCGCCTGTGGGACTACGGCATGAGCAGCAGCCCCCAGTGCTGCGCAACCGC
 311> TyrPheIleAlaAlaValGluArgLeuTrpAspTyrGlyMetSerSerSerProHisValLeuArgAsnArg
 2521 GCCCAGAGCGGCAGCGTGCCCCAGTTCAAGAAGGTGGTGTTCAGGAGTTCACCGACGGCAGCTTCACCCAG
 835> AlaGlnSerGlySerValProGlnPheLysLysValValPheGlnGluPheThrAspGlySerPheThrGln

Apal

2593 CCCCTGTACCGCGCGAGCTGAACGAGCACCTGGGCCTGCTGGGCCCTACATCCGCGCCGAGGTGGAGGAC
 859> ProLeuTyrArgGlyGluLeuAsnGluHisLeuGlyLeuLeuGlyProTyrIleArgAlaGluValGluAsp

BstEII

2665 AACATCATGGTGACCTTCCGCAACCAGGCCAGCCGCCCTACAGCTTCTACAGCAGCCTGATCAGCTACGAG
 883> AsnIleMetValThrPheArgAsnGlnAlaSerArgProTyrSerPheTyrSerSerLeuIleSerTyrGlu
 2737 GAGGACCAGCGCCAGGGCGCCGAGCCCCGCAAGAAGCTTCGTGAAGCCCAACGAGACCAAGACCTACTTCTGG
 907> GluAspGlnArgGlnGlyAlaGluProArgLysAsnPheValLysProAsnGluThrLysThrTyrPheTrp
 2809 AAGGTGCAGCACCATGGCCCCACCAAGGACGAGTTCGACTGCAAGGCCTGGGCCTACTTCAGCGACGCTG
 931> LysValGlnHisHisMetAlaProThrLysAspGluPheAspCysLysAlaTrpAlaTyrPheSerAspVal

FIG. 7 (2 of 3)

2381 TACCTGGAGAAGGACGTGCACAGCGGCCTGATCGGGCCCCCTGCTGGTGTGCCACACCAACACCCCTGAACCCC
955▶ AspLeuGluLysAspValHisSerGlyLeuIleGlyProLeuLeuValCysHisThrAsnThrLeuAsnPro

EagI BstEII

2953 GCCCAGCGCCGCCAGGTGACCGTGCAGGAGTTCCGCCCTGTTCTTCACCATCTTCGACGAGACCAAGAGCTGG
979▶ AlaHisGlyArgGlnValThrValGlnGluPheAlaLeuPhePheThrIlePheAspGluThrLysSerTrp
3025 TACTTCACCGAGAACATGGAGCGCACTGCCGCGCCCCCTGCAACATCCAGATGGAGGACCCACCTTCAAG
1003▶ TyrPheThrGluAsnMetGluArgAsnCysArgAlaProCysAsnIleGlnMetGluAspProThrPheLys
3097 GAGAACTACCGCTTCCACGCCATCAACGGCTACATCATGGACACCCCTGCCCGGCTGGTGTATGGCCCAGGAC
1027▶ GluAsnTyrArgPheHisAlaIleAsnGlyTyrIleMetAspThrLeuProGlyLeuValMetAlaGlnAsp

KpnI

PmlI

3169 CAGCGCATCCGCTGGTACCTGCTGAGCATGGGCAGCAACGAGAATCCACAGCATCCACTTCAGCGGCCAC
1051▶ GlnArgIleArgTrpTyrLeuLeuSerMetGlySerAsnGluAsnIleHisSerIleHisPheSerGlyHis
3241 GTGTTACCGTGGCAGAAGAGGAGGTACAAGATGGCCCTGTACAACCTGTACCCCGGCGTGTTCGAGACC
1075▶ ValPheThrValArgLysLysGluGluTyrLysMetAlaLeuTyrAsnLeuTyrProGlyValPheGluThr
3313 GTGGAGATGCTGCCCAGCAAGGCCGGCATCTGGCGCGTGGAGTGCCTGATCGGCGAGCACCTGCACGCCGGC
1099▶ ValGluMetLeuProSerLysAlaGlyIleTrpArgValGluCysLeuIleGlyGluHisLeuHisAlaGly
3385 ATGAGCACCCCTGTTCTCTGGTGTACAGCAACAAGTGGCAGACCCCTGGGCATGGCCAGCGGCCACATCCGC
1123▶ MetSerThrLeuPheLeuValTyrSerAsnLysCysGlnThrProLeuGlyMetAlaSerGlyHisIleArg

Apal

3457 GACTTCCAGATCACCGCCAGCGGCCAGTACGGCCAGTGGGCCCCCAAGCTGGCCCCGCTGCACTACAGCGGC
1147▶ AspPheGlnIleThrAlaSerGlyGlnTyrGlyGlnTrpAlaProLysLeuAlaArgLeuHisTyrSerGly
3529 AGCATCAACGCCTGGAGCACCAAGGAGCCCTTCAGCTGGATCAAGGTGGACCTGCTGGCCCCCATGATCATC
1171▶ SerIleAsnAlaTrpSerThrLysGluProPheSerTrpIleLysValAspLeuLeuAlaProMetIleIle
3601 CACGGCATCAAGACCCAGGGCGCCCGCCAGAAGTTCAGCAGCCTGTACATCAGCCAGTTCATCATCATGTAC
1195▶ HisGlyIleLysThrGlnGlyAlaArgGlnLysPheSerSerLeuTyrIleSerGlnPheIleIleMetTyr
3673 AGCCTGGACGGCAAGAAGTGGCAGACCTACCGCGGCAACAGCACCGGCACCCTGATGGTGTCTTCGGCAAC
1219▶ SerLeuAspGlyLysLysTrpGlnThrTyrArgGlyAsnSerThrGlyThrLeuMetValPhePheGlyAsn

(SmaI/EcoRV)

3745 GTGGACAGCAGCGGCATCAAGCACACATCTTCAACCCCCCATCATCGCCCCGTACATCCGCCTGCACCCC
1243▶ ValAspSerSerGlyIleLysHisAsnIlePheAsnProProIleIleAlaArgTyrIleArgLeuHisPro
3817 ACCCACTACAGCATCCGCAGCACCCCTGCGCATGGAGCTGATGGGCTGCGACCTGAACAGCTGCAGCATGCCC
1267▶ ThrHisTyrSerIleArgSerThrLeuArgMetGluLeuMetGlyCysAspLeuAsnSerCysSerMetPro
3889 CTGGGCATGGAGAGCAAGGCCATCAGCGACGCCCAGATCACCGCCAGCAGCTACTTCACCAACATGTTCCGCC
1291▶ LeuGlyMetGluSerLysAlaIleSerAspAlaGlnIleThrAlaSerSerTyrPheThrAsnMetPheAla
3961 ACCTGGAGCCCCAGCAAGGCCCGCCTGCACCTGCAGGGCCGAGCAACGCCTGGCGCCCCCAGGTGAACAAC
1315▶ ThrTrpSerProSerLysAlaArgLeuHisLeuGlnGlyArgSerAsnAlaTrpArgProGlnValAsnAsn

BstEII

4033 CCCAAGGAGTGGCTGCAGGTGGACTTCCAGAAGACCATGAAGGTGACCGGCGTGACCAACCAGGGCGTGAAG
1339▶ ProLysGluTrpLeuGlnValAspPheGlnLysThrMetLysValThrGlyValThrThrGlnGlyValLys
4105 AGCCTGCTGACCAGCATGTACGTGAAGGAGTTCCTGATCAGCAGCAGCCAGGACGGCCACCAAGTGGACCCCTG
1363▶ SerLeuLeuThrSerMetTyrValLysGluPheLeuIleSerSerSerGlnAspGlyHisGlnTrpThrLeu
4177 TTCTTCCAGAACGGCAAGGTGAAGGTGTTCCAGGGCAACAGGACAGCTTCAACCCCGTGGTGAACAGCCTG
1387▶ PhePheGlnAsnGlyLysValLysValPheGlnGlyAsnGlnAspSerPheThrProValValAsnSerLeu
4249 GACCCCCCCTGCTGACCCGCTACCTGCGCATCCACCCCCAGAGCTGGGTGCACCAGATCGCCCTGCGCATG
1411▶ AspProProLeuLeuThrArgTyrLeuArgIleHisProGlnSerTrpValHisGlnIleAlaLeuArgMet

SmaI

HindIII

4321 CAGGTGCTGGGCTGCGAGGCCCCAGGACCTGTACTAGCTGCCCGGGCTACAAGCTTT
1435▶ GluValLeuGlyCysGluAlaGlnAspLeuTyr...

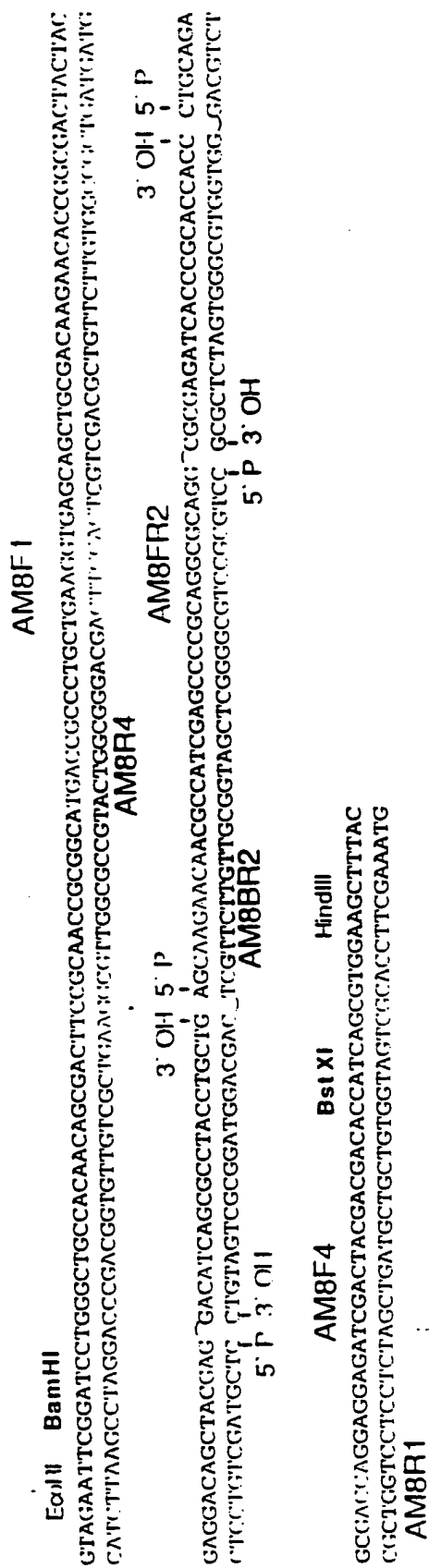


FIG. 8

1441 CAGGTGGGCGACACCCTGCTGATCATCTTCAAGAACCAGGCCAGCCGCCCCCTACAACATCTACCCCCACGGC
 475▶ GluValGlyAspThrLeuLeuIleIlePheLysAsnGlnAlaSerArgProTyrAsnIleTyrProHisGly
 1513 ATCACCACGCTGCGCCCCCTGTACAGCCGCGCCTGCCCAAGGGCGTGAAGCACCTGAAGGACTTCCCCATC
 499▶ IleThrAspValArgProLeuTyrSerArgArgLeuProLysGlyValLysHisLeuLysAspPheProIle

BglII

1585 CTGCCCCGGCGAGATCTTCAAGTACAAGTGGACCGTGACCGTGAGGACGGCCCCCAAGAGCGACCCCCCGC
 523▶ LeuProGlyGluIlePheLysTyrLysTrpThrValThrValGluAspGlyProThrLysSerAspProArg
 1657 TGCCTGACCCGCTACTACAGCAGCTTCGTGAACATGGAGCGCGACCTGGCCAGCGGCGCTGATCGGCCCCCTG
 547▶ CysLeuThrArgTyrTyrSerSerPheValAsnMetGluArgAspLeuAlaSerGlyLeuIleGlyProLeu
 1729 CTGATCTGCTACAAGGAGAGCGTGGACCAGCGCGGCAACCAGATCATGAGCGACAAGCGCAACGTGATCCTG
 571▶ LeuIleCysTyrLysGluSerValAspGlnArgGlyAsnGlnIleMetSerAspLysArgAsnValIleLeu

KpnI

1801 TTCAGCGTGTTCGACGAGAACCAGCAGCTGGTACCTGACCGAGAACATCCAGCGCTTCTGCCCAACCCCGCC
 595▶ PheSerValPheAspGluAsnArgSerTrpTyrLeuThrGluAsnIleGlnArgPheLeuProAsnProAla
 1873 GCGGTGCAGCTGGAGGACCCGAGTTCCAGGCCAGCAACATCATGCACAGCATCAACGGCTACGTGTTTCGAC
 619▶ GlyValGlnLeuGluAspProGluPheGlnAlaSerAsnIleMetHisSerIleAspGlyTyrValPheAsp
 1945 AGCCTGCAGCTGAGCGTGTGCCTGCACGAGGTGGCCTACTGGTACATCCTGAGCATCGGCGCCCGAGACCGAC
 643▶ SerLeuGlnLeuSerValCysLeuHisGluValAlaTyrTrpTyrIleLeuSerIleGlyAlaGlnThrAsp
 2017 TTCCTGAGCGTGTTCCTCAGCGGCTACACCTTCAAGCACAAGATGGTGTACGAGGACACCCTGACCCTGTTC
 667▶ PheLeuSerValPhePheSerGlyTyrThrPheLysHisLysMetValTyrGluAspThrLeuThrLeuPhe

BamHI

2089 CCCTTCAGCGGCGAGACCGTGTTCATGAGCATGGAGAACCCTGGGCTGTGGATCCTGGGCTGCCACAACAGC
 691▶ ProPheSerGlyGluThrValPheMetSerMetGluAsnProGlyLeuTrpIleLeuGlyCysHisAsnSer
 2161 GACTTCCGCAACCGCGGCATGACCGCCCTGCTGAAGGTGAGCAGCTGCGACAAGAACACCGGCGACTACTAC
 715▶ AspPheArgAsnArgGlyMetThrAlaLeuLeuLysValSerSerCysAspLysAsnThrGlyAspTyrTyr
 2233 GAGGACAGCTACGAGGACATCAGCGCCTACCTGCTGAGCAAGAACAACGCCATCGAGCCCCGCGAGGCGCAGG
 739▶ GluAspSerTyrGluAspIleSerAlaTyrLeuLeuSerLysAsnAsnAlaIleGluProArgArgArgArg

BstXI

2305 CCGGAGATCACC CGCACCACCCTGCAGAGCGACCAGGAGGAGATCGACTACGACGACACCATCAGCGTGGAG
 763▶ ArgGluIleThrArgThrThrLeuGlnSerAspGlnGluGluIleAspTyrAspAspThrIleSerValGlu
 2377 ATGAAGAAGGAGGACTTCGACATCTACGACGAGGACGAGAACCAGAGCCCCCGCAGCTTCCAGAAGAAGACC
 787▶ MetLysLysGluAspPheAspIleTyrAspGluAspGluAsnGlnSerProArgSerPheGlnLysLysThr

PmlI

2449 CCGCACTACTTCATCGCCGCGTGGAGCGCCTGTGGGACTACGGCATGAGCAGCAGCCCCACGTGCTGCGC
 811▶ ArgHisTyrPheIleAlaAlaValGluArgLeuTrpAspTyrGlyMetSerSerSerProHisValLeuArg
 2521 AACCGCGCCCAGAGCGGCAGCGTGGCCCGAGTTCAAGAAGGTGGTGTTCAGGAGTTCACCGACGGCAGCTTC
 835▶ AsnArgAlaGlnSerGlySerValProGlnPheLysLysValValPheGlnGluPheThrAspGlySerPhe

Apal

2593 ACCCAGCCCCCTGTACCGCGGCGAGCTGAACGAGCACCTGGGCCTGCTGGGCCCCCTACATCCGCGCCGAGGTG
 359▶ ThrGlnProLeuTyrArgGlyGluLeuAsnGluHisLeuGlyLeuLeuGlyProTyrIleArgAlaGluVal

BstEII

2665 CAGGACAACATCATGGTGACCTTCCGCAACCAGGCCAGCCGCCCCCTACAGCTTCTACAGCAGCCTGATCAGC
 383▶ GluAspAsnIleMetValThrPheArgAsnGlnAlaSerArgProTyrSerPheTyrSerSerLeuIleSer
 2737 TACGAGGAGGACCGAGCGCCAGGGCGCCGAGCCCCCGCAGAAGTTCGTGAAGCCCCACGAGACCAAGACCTAC
 907▶ TyrGluGluAspGlnArgGlnGlyAlaGluProArgLysAsnPheValLysProAsnGluThrLysThrTyr
 2809 TTCTGGAAGGTGCAGCACCATGGCCCCACCAAGGACGAGTTCGACTGCAAGGCCTGGGCCTACTTCAGC
 931▶ PheTrpLysValGlnHisHisMetAlaProThrLysAspGluPheAspCysLysAlaTrpAlaTyrPheSer

2681 CACGTGGACCTGGAGAAGGACGTGCACAGCGGCCTGATCGGCCCCCTGCTGGTGTGCCACACCAACACCCCTG
 955▶ AspValAspLeuGluLysAspValHisSerGlyLeuIleGlyProLeuLeuValCysHisThrAsnThrLeu

EagI BstEII

2953 AACCCCGCCCCACGGCCGCCAGGTGACCGTGCAGGAGTTCCGCCCTGTTCTTCACCATCTTCGACGAGACCAAG
 979▶ AsnProAlaHisGlyArgGlnValThrValGlnGluPheAlaLeuPhePheThrIlePheAspGluThrLys

3025 AGCTGGTACTTCACCGAGAACATGGAGCGCACTGCCGCGCCCCCTGCAACATCCAGATGGAGGACCCACCC
 1003▶ SerTrpTyrPheThrGluAsnMetGluArgAsnCysArgAlaProCysAsnIleGlnMetGluAspProThr

3097 TTCAAGGAGAACTACCGCTTCCACGCCATCAACGGCTACATCATGGACACCCCTGCCCGGCCTGGTGATGGCC
 1027▶ PheLysGluAsnTyrArgPheHisAlaIleAsnGlyTyrIleMetAspThrLeuProGlyLeuValMetAla

KpnI

3169 CAGGACCAGCGCATCCGCTGGTACCTGCTGAGCATGGGCAGCAACGAGAACATCCACAGCATCCACTTCAGC
 1051▶ GlnAspGlnArgIleArgTrpTyrLeuLeuSerMetGlySerAsnGluAsnIleHisSerIleHisPheSer

PmlI

3241 GGCCACGTGTTACCGTGCCTCAAGAAGGAGGAGTACAAGATGGCCCTGTACAACCTGTACCCCGGCGTGTTTC
 1075▶ GlyHisValPheThrValArgLysLysGluGluTyrLysMetAlaLeuTyrAsnLeuTyrProGlyValPhe

3313 GAGACCGTGGAGATGCTGCCAGCAAGGCCGGCATCTGGCGCGTGGAGTGCCTGATCGGCGAGCACCTGCAC
 1099▶ GluThrValGluMetLeuProSerLysAlaGlyIleTrpArgValGluCysLeuIleGlyGluHisLeuHis

3385 CCGGCGCATGAGCACCCCTGTTCTGCTGTACAGCAACAAGTGCCAGACCCCCCTGGGCATGGCCAGCGGCCAC
 1123▶ AlaGlyMetSerThrLeuPheLeuValTyrSerAsnLysCysGlnThrProLeuGlyMetAlaSerGlyHis

Apal

3457 ATCCGCGACTTCCAGATCACCGCCAGCGGCCAGTACGGCCAGTGGGCCCCCAAGCTGGCCCGCCTGCACTAC
 1147▶ IleArgAspPheGlnIleThrAlaSerGlyGlnTyrGlyGlnTrpAlaProLysLeuAlaArgLeuHisTyr

3529 AGCGGCAGCATCAACGCCTGGAGCACCAGGAGCCCTTCAGCTGGATCAAGGTGGACCTGCTGGCCCCCATG
 1171▶ SerGlySerIleAsnAlaTrpSerThrLysGluProPheSerTrpIleLysValAspLeuLeuAlaProMet

3601 ATCATCCACGGCATCAAGACCCAGGGCGCCCGCCAGAAGTTCAGCAGCCTGTACATCAGCCAGTTTCATCATC
 1195▶ IleIleHisGlyIleLysThrGlnGlyAlaArgGlnLysPheSerSerLeuTyrIleSerGlnPheIleIle

3673 ATGTACAGCCTGGACGGCAAGAAGTGGCAGACCTACCGCGGCAACAGCACCGGCACCCTGATGGTGTCTTCTC
 1219▶ MetTyrSerLeuAspGlyLysLysTrpGlnThrTyrArgGlyAsnSerThrGlyThrLeuMetValPhePhe

(SmaI/EcoRV)

3745 GGCAACGTGGACAGCAGCGGCATCAAGCACAACATCTTCAACCCCCCATCATCGCCCGCTACATCCGCCTG
 1243▶ GlyAsnValAspSerSerGlyIleLysHisAsnIlePheAsnProProIleIleAlaArgTyrIleArgLeu

3817 CACCCACCCACTACAGCATCCGCAGCACCCCTGCGCATGGAGCTGATGGGCTGCGACCTGAACAGCTGCAGC
 1267▶ HisProThrHisTyrSerIleArgSerThrLeuArgMetGluLeuMetGlyCysAspLeuAsnSerCysSer

3889 ATGCCCCCTGGGCATGGAGAGCAAGGCCATCAGCGACGCCCAGATCACCGCCAGCAGCTACTTCACCAACATG
 1291▶ MetProLeuGlyMetGluSerLysAlaIleSerAspAlaGlnIleThrAlaSerSerTyrPheThrAsnMet

3961 TTCGCCACCTGGAGCCCCAGCAAGGCCCGCTGCACCTGCAGGGCCCCAGCAACGCCTGGCGCCCCCAGGTG
 1315▶ PheAlaThrTrpSerProSerLysAlaArgLeuHisLeuGlnGlyArgSerAsnAlaTrpArgProGlnVal

BstEII

4033 AACAAACCCCAAGGAGTGGCTGCAGGTGGACTTCCAGAAGACCATGAAGGTGACCGGCGTGACCACCCAGGGC
 1339▶ AsnAsnProLysGluTrpLeuGlnValAspPheGlnLysThrMetLysValThrGlyValThrThrGlnGly

4105 GTGAAGAGCCTGCTGACCAGCATGTACGTGAAGGAGTTCTCTGATCAGCAGCAGCCAGGACGGCCACCAGTGG
 1363▶ ValLysSerLeuLeuThrSerMetTyrValLysGluPheLeuIleSerSerSerGlnAspGlyHisGlnTrp

4177 ACCCTGTTCTTCCAGAACGGCAAGGTGAAGGTGTTCCAGGGCAACCAGGACAGCTTCACCCCGTGGTGAAC
 1387▶ ThrLeuPhePheGlnAsnGlyLysValLysValPheGlnGlyAsnGlnAspSerPheThrProValValAsn

4249 AGCCTGGACCCCCCTGCTGACCCGCTACCTGCGCATCCACCCCGAGAGCTGGGTGCACCAGATCGCCCTG
 1411▶ SerLeuAspProProLeuLeuThrArgTyrLeuArgIleHisProGlnSerTrpValHisGlnIleAlaLeu

SmaI

HindIII

4321 CGCATCGAGGTGCTGGGCTGCGAGGCCAGGACCTGTACTAGCTGCCCGGGCTACAAGCTTTAC
 1435▶ ArgMetGluValLeuGlyCysGluAlaGlnAspLeuTyr...

FIG. 9 (3 of 3)

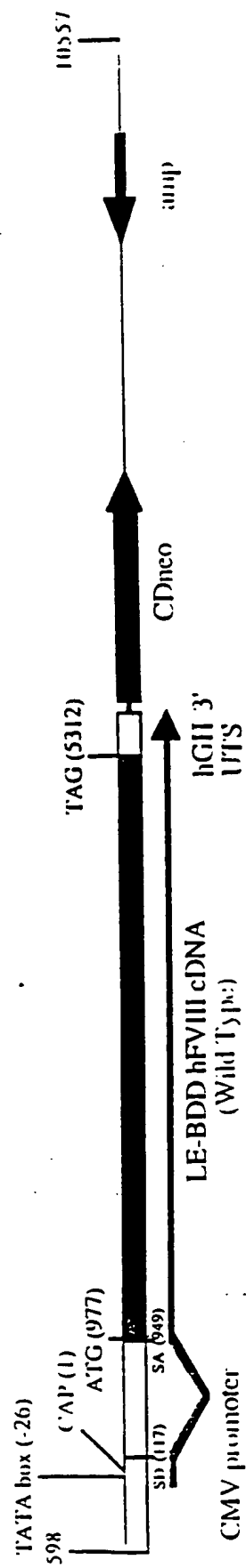


FIG. 10

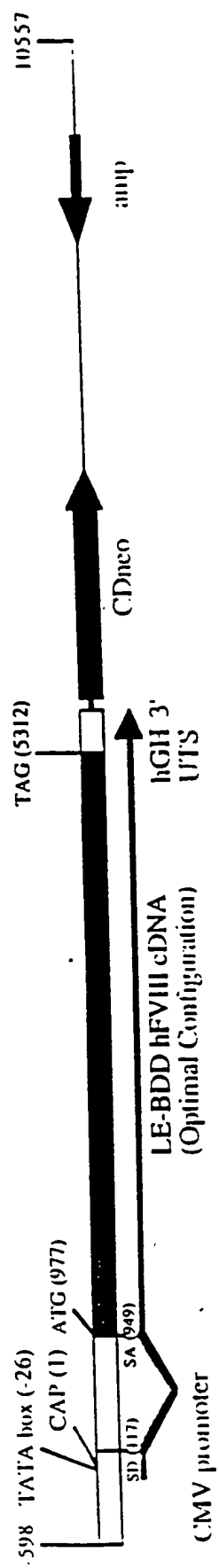


FIG. 11

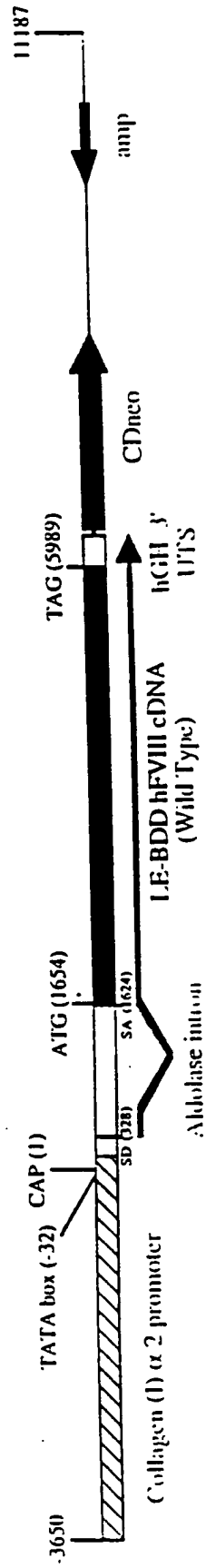


FIG. 12

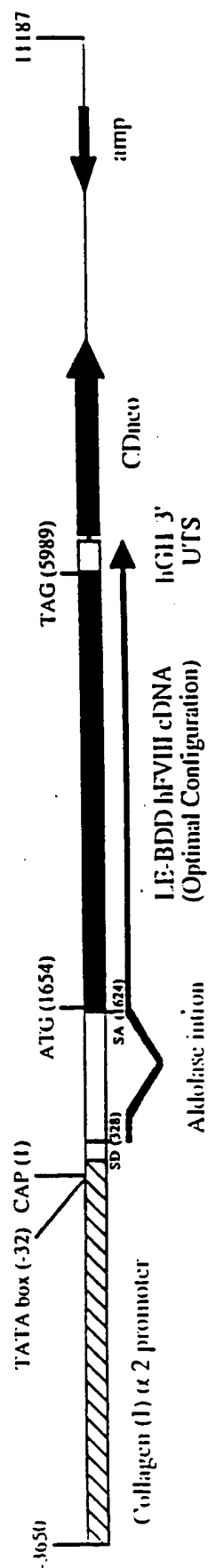


FIG. 13

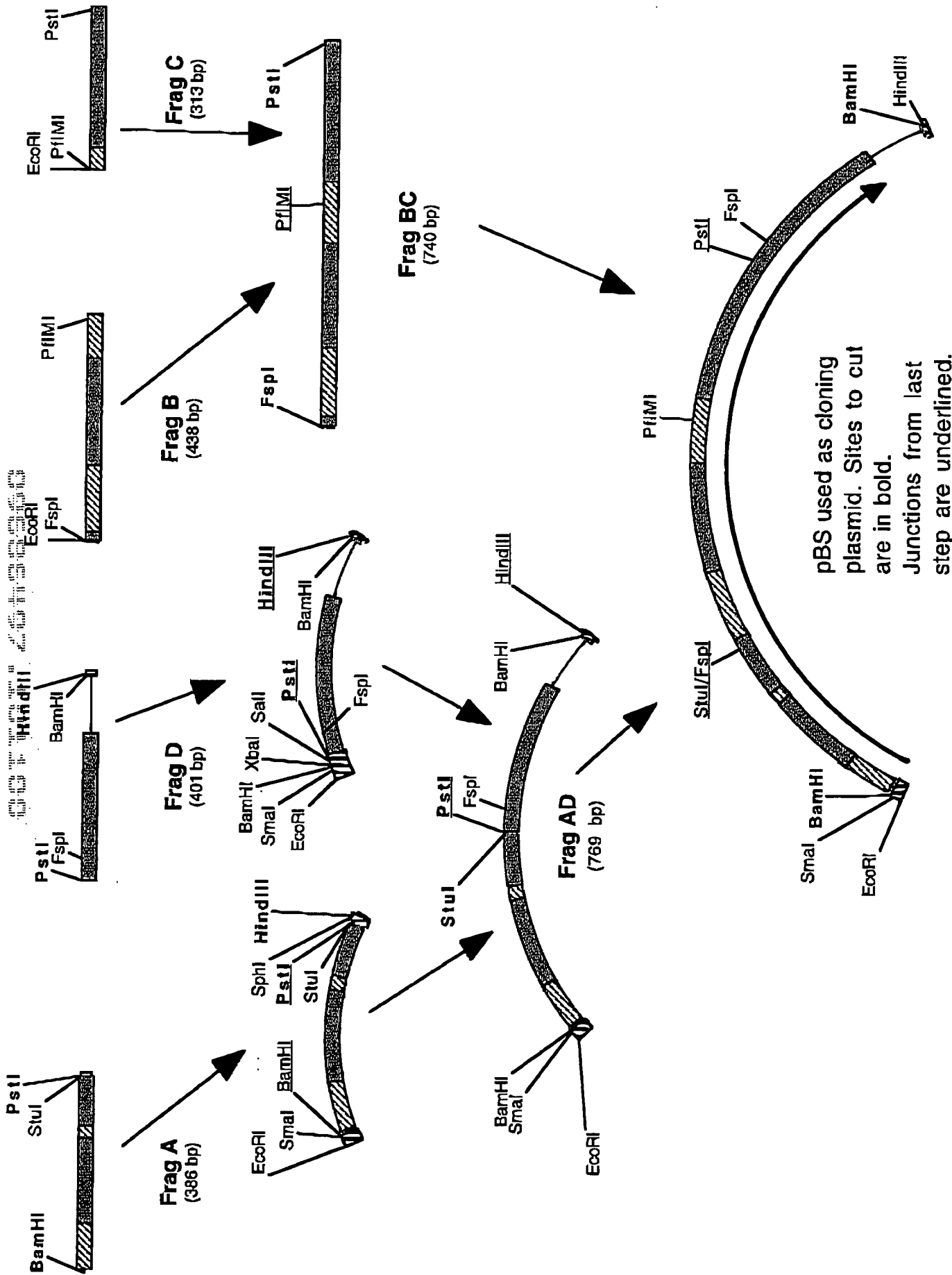


Fig. 14

GGATCCATGCAGCGCGTGAACATGATCATGGCCGAGAGCCCCGGCCTGATCACCATCTG
CCTGCTGGGCTACCTGCTGAGCGCCGAGTGACCGTGTTCTTGACCACGAGAACGCCA
ACAAGATCCTGAACCGCCCCAAGCGCTACAACAGCGGCAAGCTGGAGGAGTTCGTGCAG
GGCAACCTGGAGCGCGAGTGCATGGAGGAGAAGTGCAGCTTCGAGGAGGCCCGCGAGGT
GTTGAGAACACCGAGCGCACCACCGAGTTCTGGAAGCAGTACGTGGACGGCGACCAGT
GCGAGAGCAACCCCTGCCTGAACGGCGGCAGCTGCAAGGACGACATCAACAGCTACGAG
TGC TGGTGCCCTTCGGCTTCGAGGGCAAGAACTGCGAGCTGGACGTGACCTGCAACAT
CAAGAACGGCCGCTGCGAGCAGTTCTGCAAGAACAGCGCCGACAACAAGGTGGTGTGCA
GCTGCACCGAGGGCTACCGCCTGGCCGAGAACCAGAAGAGCTGCGAGCCCCGCCGTGCCC
TTCCCCTGCGGCCGCGTGAGCGTGAGCCAGACCAGCAAGCTGACCCGCGCCGAGACCGT
GTTCCCCGACGTGGACTACGTGAACAGCACCGAGGCCGAGACCATCCTGGACAACATCA
CCCAGAGCACCCAGAGCTTCAACGACTTCACCCGCGTGGTGGGCGGCGAGGACGCCAAG
CCCGGCCAGTTCCCCTGGCAGGTGGTGCTGAACGGCAAGGTGGACGCCTTCTGCGGCGG
CAGCATCGTGAACGAGAAGTGGATCGTGACCGCCGCCACTGCGTGGAGACCGGCGTGA
AGATCACCGTGGTGGCCGGCGAGCACACATCGAGGAGACCGAGCACACCGAGCAGAAG
CGCAACGTGATCCGCATCATCCCCACCACAACCTACAACGCCGCCATCAACAAGTACAA
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CCATCTGCATCGCCGACAAGGAGTACACCAACATCTTCCTGAAGTTCGGCAGCGGCTAC
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ACAACATGTTCTGCGCCGGCTTCCACGAGGGCGGCCGCGACAGCTGCCAGGGCGACAGC
GGCGGCCCCACGTGACCGAGGTGGAGGGCACCAGCTTCCTGACCGGCATCATCAGCTG
GGGCGAGGAGTGCGCCATGAAGGGCAAGTACGGCATCTACACCAAGGTGAGCCGCTACG
TGAAGTGGATCAAGGAGAAGACCAAGCTGACCTAATGAAAGATGGATTTCCAAGGTTAA
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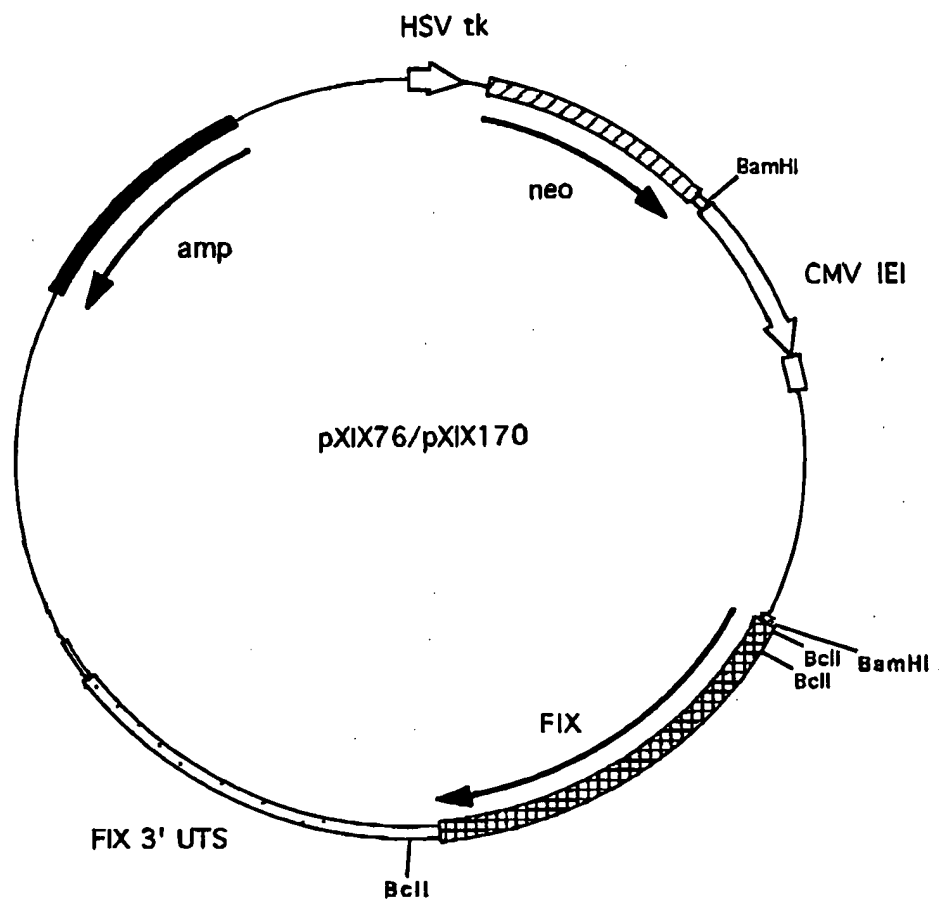


Fig. 16

GGATCCGCTAGAGCGGAAATTTATGCTGTCCGGTCACCGTGACAATGCAGCTGCGCAAC
CCCGAGCTGCACCTGGGCTGCGCCCTGGCCCTGCGCTTCCTGGCCCTGGTGAGCTGGGA
CATCCCCGGCGCCCGCGCCCTGGACAACGGCCTGGCCCGCACCCCCACCATGGGCTGGC
TGCACTGGGAGCGCTTCATGTGCAACCTGGACTGCCAGGAGGAGCCCCGACAGCTGCATC
AGCGAGAAGCTGTTCATGGAGATGGCCGAGCTGATGGTGAGCGAGGGCTGGAAGGACGC
CGGCTACGAGTACCTGTGCATCGACGACTGCTGGATGGCCCCCAGCGCGACAGCGAGG
GCCGCCTGCAGGCCGACCCCCAGCGCTTCCCCACGGCATCCGCCAGCTGGCCAACTAC
GTGCACAGCAAGGGCCTGAAGCTGGGCATCTACGCCGACGTGGGCAACAAGACCTGCGC
CGGCTTCCCCGGCAGCTTCGGCTACTACGACATCGACGCCCAGACCTTCGCCGACTGGG
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GGCTACAAGCACATGAGCCTGGCCCTGAACCGCACCGGCCGAGCATCGTGTACAGCTG
CGAGTGGCCCCTGTACATGTGGCCCTTCCAGAAGCCCAACTACACCGAGATCCGCCAGT
ACTGCAACCACTGGCGCAACTTCGCCGACATCGACGACAGCTGGAAGAGCATCAAGAGC
ATCCTGGACTGGACCAGCTTCAACCAGGAGCGCATCGTGGACGTGGCCGGCCCCGGCGG
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TGACCCAGATGGCCCTGTGGGCCATCATGGCCGCCCCCCTGTTTCATGAGCAACGACCTG
CGCCACATCAGCCCCCAGGCCAAGGCCCTGCTGCAGGACAAGGACGTGATCGCCATCAA
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CCCCGCCTGCTTCATACCCAGCTGCTGCCCGTGAAGCGCAAGCTGGGCTTCTACGAGT
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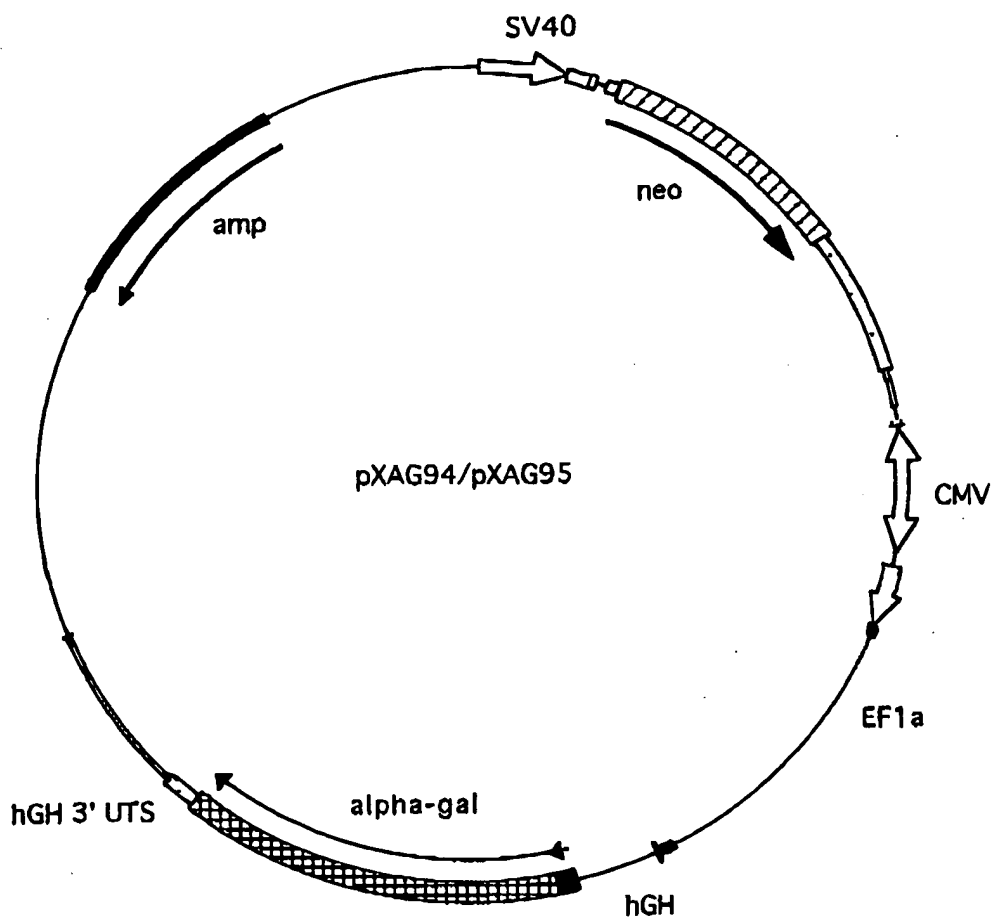


Fig 18

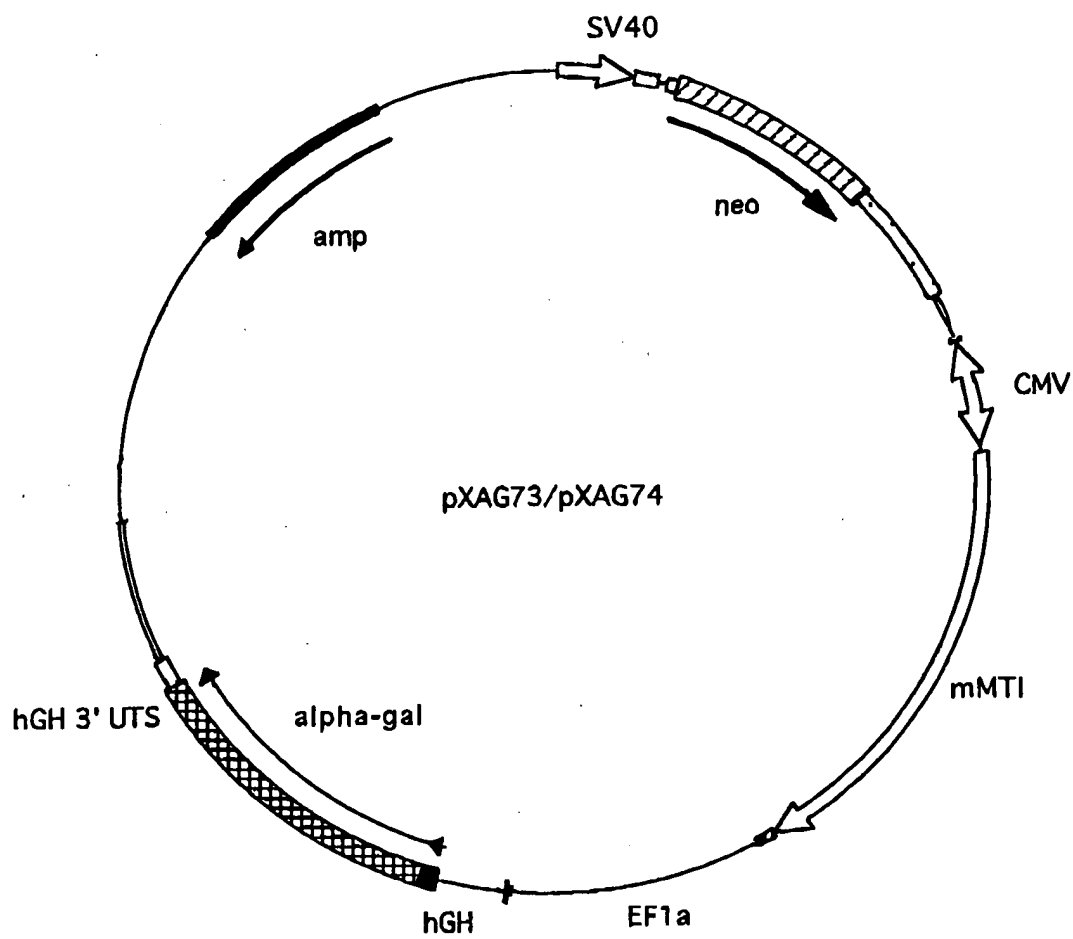


Fig. 19